

Bjarne Duc Larsen  
USSN: 09/341,590  
Page 2

#### AMENDMENTS TO THE CLAIMS:

The present listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-81 (previously canceled).

Claim 82. (currently amended) A peptide conjugate consisting of X and Z,

wherein X is a pharmacologically active peptide sequence, and

wherein Z is a stabilising peptide sequence [of 4-20 amino acid units] covalently bound by its N terminus to the C terminus end of X, wherein Z is  $\text{Lys}_p\text{-Xaa}_q$  or  $\text{Xaa}_p\text{-Lys}_q$ , wherein p and q are integers in the range from 1 to 14, with the proviso that p+q is in the range of 4-15, and each Xaa is Ser, Thr, Tyr, Asn, Gln, Asp, Glu, Arg, His, Orn, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid or Met; or a salt thereof,

wherein,

X is selected from the group consisting of AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala) (SEQ ID NO: 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) (SEQ ID NO: 15), insulin-like growth factor I (30-41) (Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 16), insulin-like growth factor I (24-41) (Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 17), insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 18), insulin-like growth factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 19), insulin-like growth factor II (69-84) (Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro-Arg-Tyr) (SEQ ID NO: 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) (His-DTrp-Ala-Trp-DPhe-Lys-NH<sub>2</sub>) (SEQ ID NO: 21), beta-Interleukin I (163-171) (Val-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) (SEQ ID NO: 22), beta-Interleukin II (44-56) (Ile-Leu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) (SEQ ID NO: 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) (SEQ ID NO: 24),

Bjarne Duc Larsen  
USSN: 09/341,590  
Page 3

exendin-4 (GLP-1 analog) (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH<sub>2</sub>) (SEQ ID NO: 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Ser) (SEQ ID NO: 26), epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) (SEQ ID NO: 27), bivalirudin (Hirulog) (D-Phe-Pro-Arg-Pro-(Gly)<sub>4</sub>-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu) (SEQ ID NO: 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)<sub>4</sub>-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Leu (SEQ ID NO: 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Trp-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Leu-Gly-Cys; Disulfide bridge: Cys37-Cys53) (SEQ ID NO: 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Arg, disulfide bridge cys2-cys13) (SEQ ID NO: 31), Melanotan-II (MT-II, alpha-MSH4-10-NH<sub>2</sub>, or Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) (SEQ ID NO: 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn) (SEQ ID NO: 33), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Om-Gly-NH<sub>2</sub>, Disulfide bridge: Cys1-Cys6) (SEQ ID NO: 34), octreotide (201-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thr-ol; disulfide bridge: Cys2-Cys7) (SEQ ID NO: 35), calcitonin gene-related peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH<sub>2</sub>; Disulfide bridge: Cys2-Cys7) (SEQ ID NO: 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH<sub>2</sub> (SEQ ID NO: 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH<sub>2</sub> (SEQ ID NO: 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) (SEQ ID NO: 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His) (SEQ ID NO: 40), adrenomedullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg) (SEQ ID NO: 41), antiarrhythmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) (SEQ ID NO: 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH<sub>2</sub>), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Tip-Pro-Trp-Arg-Arg-NH<sub>2</sub>) (SEQ ID NO: 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) (SEQ ID NO: 44), cortistatin 29 (1-13)

Bjarne Due Larsen  
 USSN: 09/341,590  
 Page 4

(Glp)-Glu-Arg-Pro-Pro-Leu-Gln-Gln-Pro-Pro-His-Arg-Asp) (SEQ ID NO: 45), cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide bridge: Cys2-Cys13 (SEQ ID NO: 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH<sub>2</sub>) (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH<sub>2</sub>) (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn (SEQ ID NO: 54), Leupeptin (Ac-Leu-Lcu-Arg-CHO); and Leu-enkephalin-Lys-Glu-Glu-Glu-Glu-Lys-OH) (SEQ ID NO: 98) or a modified or truncated analogue of X having at least about 5 and up to at most about 75 amino acids.

Claim 83. (previously presented) A peptide conjugate comprising X and Z,

wherein X is a pharmacologically active peptide sequence, and

wherein Z is a stabilising peptide having the following sequence: Lys<sub>4-10</sub> units covalently bound by its N terminus to the C terminus end of X ; or a salt thereof,

wherein,

X is selected from the group consisting of AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala) (SEQ ID NO: 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) (SEQ ID NO: 15), insulin-like growth factor I (30-41) (Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 16), insulin-like growth factor I (24-41) (Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO: 17), insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 18), insulin-like growth factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO: 19), insulin-like growth factor II (69-84) (Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro-Arg-Tyr) (SEQ ID NO: 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) (His-DTrp-Ala-Trp-DPhe-Lys-NH<sub>2</sub>) (SEQ ID NO: 21), beta-

Bjarné Due Larsen  
USSN: 09/341,590  
Page 5

Interleukin I (163-171) (Val-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) (SEQ ID NO: 22), beta-Interleukin II (44-56) (Ile-Leu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) (SEQ ID NO: 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) (SEQ ID NO: 24), exendin-4 (GLP-1 analog) (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Lcu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Ser-NH<sub>2</sub>) (SEQ ID NO: 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Ser) (SEQ ID NO: 26), epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) (SEQ ID NO: 27), bivalirudin (Hirulog) (D-Phe-Pro-Arg-Pro-(Gly)<sub>4</sub>-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Lcu) (SEQ ID NO: 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)<sub>4</sub>-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Lcu (SEQ ID NO: 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Trp-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Lcu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Lcu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Lcu-Gly-Cys; Disulfide bridge: Cys37-Cys53) (SEQ ID NO: 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Arg, disulfide bridge cys2-cys13) (SEQ ID NO: 31), Melanotan-II (MT-II, alpha-MSH4-10-NH<sub>2</sub>, or Ac-Nle4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) (SEQ ID NO: 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn) (SEQ ID NO: 33), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Orn-Gly-NH<sub>2</sub>, Disulfide bridge: Cys1-Cys6) (SEQ ID NO: 34), octreotide (201-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thr-ol; disulfide bridge: Cys2-Cys7) (SEQ ID NO: 35), calcitonin gene-related peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-Ile-Arg-Lcu-Ala-Gly-Lcu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Asn-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH<sub>2</sub>; Disulfide bridge: Cys2-Cys7) (SEQ ID NO: 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH<sub>2</sub> (SEQ ID NO: 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH<sub>2</sub> (SEQ ID NO: 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) (SEQ ID NO: 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His) (SEQ ID NO: 40), adrenomedullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Lcu-Arg) (SEQ ID NO: 41), antiarrhythmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) (SEQ ID

Bjarne Due Larsen  
USSN: 09/341,590  
Page 6

NO: 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH<sub>2</sub>), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Trp-Pro-Trp-Arg-Arg-NH<sub>2</sub>) (SEQ ID NO: 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) (SEQ ID NO: 44), cortistatin 29 (1-13) (Glp)-Glu-Arg-Pro-Pro-Lcu-Gln-Gln-Pro-Pro-His-Arg-Asp) (SEQ ID NO: 45), cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide bridge: Cys2-Cys13 (SEQ ID NO: 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO: 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) (SEQ ID NO: 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) (SEQ ID NO: 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH<sub>2</sub>) (SEQ ID NO: 51) Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH<sub>2</sub>) (SEQ ID NO: 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) (SEQ ID NO: 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn (SEQ ID NO: 54), Lcu-enkephalin-Lys-Glu-Glu-Glu-Glu-Lys-OH) (SEQ ID NO: 98) and Leupeptin (Ac-Leu-Leu-Arg-CHO).

Claims 84-86 (Canceled)

Claim 87. (previously presented) A peptide conjugate according to claim 83, wherein Z is Lys4 (SEQ ID NO: 55), Lys5 (SEQ ID NO: 56) or Lys6 (SEQ ID NO: 62).

Claim 88. (previously presented) A peptide conjugate according to claim 87, wherein Z is Lys<sub>6</sub> (SEQ ID NO: 62).

Claim 89. (previously presented) A peptide conjugate according to claim 82 or 83, wherein Z consists of L-amino acids only.

Claim 90. (previously presented) A peptide conjugate represented by one of the following formulac:

Bjarne Due Larsen  
USSN: 09/341,590  
Page 7

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Lcu-Lys<sub>6</sub>-NH<sub>2</sub> (GHRH(1-44)(Human)-Lys<sub>6</sub>-NH<sub>2</sub>) (SEQ ID NO: 88);

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Lcu-Glu<sub>6</sub>-NH<sub>2</sub> (GHRH(1-44)(Human)-Glu<sub>6</sub>-NH<sub>2</sub>) (SEQ ID NO: 89);

H-Ser-Val-Ser-Glu-Ile-Glu-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-Lys<sub>6</sub>-OH (PTH(1-34)(Human)-Lys<sub>6</sub>-OH) (SEQ ID NO: 91);

H-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Lys<sub>6</sub>-OH (GLP-1-(7-36)(Human)-Lys<sub>6</sub>-OH) (SEQ ID NO: 92);

H-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-Lys<sub>6</sub>-OH (EMP-1-Lys<sub>6</sub>-OH) (SEQ ID NO: 93);

H-Aib-His-2-D-Nal-D-Phe-Lys-(Lys)<sub>6</sub>-NH<sub>2</sub> (GHRP-(Lys)<sub>6</sub>-NH<sub>2</sub>) (SEQ ID NO: 96);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Lys-Glu-Glu-Glu-Lys-OH (Leu-enkephalin-Lys-Lys-Glu-Glu-Glu-Lys-OH) (SEQ ID NO: 97);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys-OH (Leu-enkephalin-Lys-Glu-Glu-Glu-Glu-Lys-OH) (SEQ ID NO: 98);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys-OH (Leu-enkephalin-(Lys-Glu)<sub>3</sub>) (SEQ ID NO: 99);

Bjarne Due Larsen  
USSN: 09/341,590  
Page 8

H-Tyr-Gly-Gly-Phe-Leu-(Dpr)<sub>6</sub>-OH (Leu-enkephalin-(Dpr)<sub>6</sub>-OH) (SEQ ID NO: 100);

H-Tyr-Gly-Gly-Phe-Leu- Lys<sub>6</sub>-OH (H-Leu-enkephalin-Lys<sub>6</sub>) (SEQ ID NO: 11);

Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-(Lys)<sub>6</sub>-OH (GnRH-Lys<sub>6</sub>-OH) (SEQ ID NO: 103);

Glu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-(Lys-Glu)<sub>3</sub>-OH (GnRH-(Lys-Glu)<sub>3</sub>-OH) (SEQ ID NO: 104); and

H-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-(Lys-Glu)<sub>3</sub>-OH (PTH 1-34 human-(Lys-Glu)<sub>3</sub>-OH) (SEQ ID NO: 105).

Claim 91. (previously presented) A method for the preparation of a peptide conjugate (X-Z) as defined in claim 82 or 83, comprising the steps of:

- a) coupling an N- $\alpha$ -protected amino acid or N- $\alpha$ -protected dipeptide in the carboxyl activated form, in the C-terminal activated form to an immobilised peptide sequence H-Z-SSM, thereby forming an immobilised N- $\alpha$ -protected peptide fragment,
- b) removing the N- $\alpha$ -protecting group, thereby forming an immobilised peptide fragment having an unprotected N-terminal end,
- c) coupling an additional N- $\alpha$ -protected amino acid in the carboxyl activated form, or an additional N- $\alpha$ -protected dipeptide in the C-terminal activated form to the N-terminal end of the immobilised peptide fragment, and repeating the removal/coupling step procedure in step b) and c) until the desired peptide sequence X is obtained, and then
- d) cleaving off the peptide conjugate from the solid support material.

Bjarne Due Larsen  
USSN: 09/341,590  
Page 9

Claim 92. (previously presented) A method for producing the peptide conjugate of claim 82 or 83, comprising

- a) introducing a nucleic acid sequence encoding said conjugate into a host cell;
- b) culturing said host cell for a time and under conditions effective to produce said peptide conjugate, and isolating said conjugate from the culture.

Claim 93. (previously presented) A method for producing the peptide conjugate of claim 82 or 83, comprising

- a) culturing a recombinant host cell comprising a nucleic acid sequence encoding said conjugate under conditions permitting the production of said conjugate; and
- b) isolating said conjugate from the culture.

Claim 94. (previously presented) The method according to claim 92, wherein the nucleic acid sequence encoding said conjugate is contained within a nucleic acid construct or a vector.

Claim 95. (previously presented) The method according to claim 93, wherein the nucleic acid sequence encoding said conjugate is contained within a nucleic acid construct or a vector.

Claim 96. (previously presented) A composition comprising a peptide conjugate according to claim 82 or 83, and a pharmaceutical acceptable carrier.

Claim 97. (previously presented) The peptide conjugate of claim 82 or 83, wherein Z consists of about 4 to about 7 amino acid units.

Claim 98. (previously presented) The peptide conjugate of claim 97, wherein Z consists of 6 amino acid units.

Claim 99. (previously presented) The peptide conjugate of claim 82 or 83, wherein Z comprises at least five Lys amino acid units.



Bjarne Due Larsen  
USSN: 09/341,590  
Page 10

Claim 100. (previously presented) The peptide conjugate of claim 99, wherein Z comprises six Lys amino acid units.

Claim 101. (currently amended) The peptide conjugate according to claim [82 or] 83, wherein Z is (Lys)<sub>n</sub> in which n is an integer in the range from about 4 to 10.

Claim 102. (previously presented) The peptide conjugate of claim 101, wherein n is an integer in the range from about 4 to 8 or about 4 to 6.

Claim 103. (canceled).

Claim 104. (previously presented) The peptide conjugate of claim 82 or 83, wherein Z is further defined by having a free acid, amide or ester group.

Claim 105. (previously presented) A method of achieving binding between the conjugate of claim 82 or 83 and  $\mu$  opioid receptors comprising administering to the subject in need thereof the conjugate for a time and under conditions effective to achieve binding between said conjugate and  $\mu$  opioid receptors.

Claim 106. (previously presented) A composition comprising a pharmaceutically acceptable carrier and a conjugate according to claim 82 or 83 in an amount effective to bind  $\mu$  opioid receptors.

Claim 107. (previously presented) A composition comprising a pharmaceutically acceptable carrier, and a conjugate according to claim 82 or 83 in an amount effective to stimulate erythropoiesis.

Bjarne Due Larsen  
USSN: 09/341,590  
Page 11

Claim 108. (previously presented) A composition comprising a pharmaceutically acceptable carrier, and a conjugate according to claim 82 or 83 in an amount effective to induce retraction of osteoblasts.

Claim 109. (previously presented) The peptide conjugate of claim 82 or 83, wherein the conjugate is represented by the following sequence: Ac-Ser-Tyr-Ser-Met-Glu-His-Phe-Arg-Trp-Gly-Lys-Pro-Val-(Lys)<sub>6</sub>-NH<sub>2</sub> (SEQ ID NO: 122) or a fragment thereof.

Claim 110. (previously presented) The peptide conjugate of claim 82 or 83, wherein the ratio between the half-life of said peptide conjugate and the half-life of the corresponding pharmacologically active peptide sequence X, when treated with carboxypeptidase A or leucine aminopeptidase in about 50 mM phosphate buffer solution at about pH 7.4 at about 37°C or in serum or plasma is at least 2.

Claim 111. (previously presented) The peptide conjugate of claim 110, wherein the ratio is at least about 5, 7, 9, or 10.

Claims 112 - 114. (canceled)